

BOSTON UNIVERSITY

GRADUATE SCHOOL

Thesis

HYDROLYSIS OF NITROURETHANS

by

Howard Millard Curry

(B.S., Northeastern University, 1945)
submitted in partial fulfilment of the
requirements for the degree of

MASTER OF ARTS

1947

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HYDROLYSIS OF NITROURETHANS

I. INTRODUCTION

A. Historical Survey

The nitrourethans, although relatively simple in structure compared with other types of organic compounds which have been studied widely, have received very little attention from organic chemists. No more than four or five investigators have dealt with them, and then only superficially. Nitrourethans have been prepared and a few of the simpler properties determined, but at the present date the chemistry of these compounds is still in its infancy.

Probably the earliest published article on nitration of urethans was that of Thiele and Lachmann (11.) published in 1884. This nitration was performed on urethan itself by means of the following procedure:

Five-hundred cubic centimeters of pure, concentrated sulfuric acid was stirred mechanically and 100 grams of powdered urethan was added. The reaction vessel was cooled in an ice-salt bath. After all of the urethan had dissolved and the temperature had sunk below 0°C, 110 gr. of ethyl nitrate was allowed to flow in. The cooling was so regulated that the temperature remained below -5°C during the whole operation. Forty-five minutes after addition of the ethyl nitrate, the acid was poured, with stirring, onto 1.5 to 2 kg. of ice. The mixture was extracted with ether and diluted so that the total volume of the ethereal solution was about four liters.

 $c_{2}H_{5}ooc-NH_{2} \neq c_{2}H_{5}oNo_{2} \longrightarrow c_{2}H_{5}ooc-NH-No_{2} \neq c_{2}H_{5}oH$ The ammonium salt was obtained from the ethereal solution by passing in a stream of dry ammonia.

HYDROLYSIS OF NITROUGHTHANS

I. IMPRODUCTION

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C2H500C-MH2 / C2H50NO2 - - - C2H500C-NH-NO2 / C2H5OH

The ammonium salt was obtained from the ethereal solution by passing in a stream of dry ammonia.

$$c_{2}H_{5}ooc-NH-NO_{2} \neq NH_{3} \longrightarrow c_{2}H_{5}ooc-N(NH_{4})-NO_{2}$$

The ammonium salt was then dissolved in an excess of dilute sulfuric acid and the nitrourethan was extracted with ether.

$$2C_2H_5$$
 $00C-N(NH_4)-NO_2 \neq H_2SO_4 \longrightarrow 2C_2H_5$ $00C-NH-NO_2 \neq (NH_4)_2SO_4$

The other solution was dried with calcium chloride and the other was distilled on the water bath.

A more general method of nitrating substituted urethans was reported four years later by Franchimont and Klobbie (3.) Nitration of the substituted urethans was accomplished by means of a large excess of nitric acid. Details of their method as revised by Thomas (12.) appear later in this report. The main interest of these investigators was not directed toward the nitrourethans but to the decomposition of the former compounds by ammonia to yield nitroamines.

$$R-N(NO_2)-COOC_2H_5 \neq 2NH_3 \longrightarrow R-N(NO_2)(NH_4) \neq NH_2-COOC_2H_5$$

With this object in mind the following nitrourethans were prepared within the next ten years.

TABLE I
PROPERTIES OF NITROURETHANS

COMPOUND	B.P.	F.P.	Sp.gr.@ 15°C
1. Methyl ester of N-Nitro-N-n-propylcarbamic acid (12.)	139°C d.		1.187
2. Methyl ester of N-Nitro-N-isopropylcarbamic acid (12.)	120°C d.		1.1585
3. Methyl ester of N-Nitro-N-n-butylcarbamic acid (15.)		-35°0	1.149
4. Methyl ester of N-Nitro-N-secbutylcarbamic acid (15.)		below-70°C	1.1355

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PROPERTIES OF NITHOURATHANS

F.P. Sp.gr.0 15°C	B.P.	onuonio	10
1.187	139°C 8.	Nethyl ester of Mitro-N-n-propylogrosmic soid (12.)	
1,1585	.b 0°081	Mathyl aster of N-Nitro-N-isograpylesrbamic sold (12.)	2.
-35°C 1.149		To refee Lydfell (15.)	3.
below-70°C 1.1355		(.21) bise simedraplyjud-secW-witto-W-was (.25)	4.

TABLE I (cont.)

COMPOUND	B.P.	F.P.	Sp.gr.@ 15°C
5. Ethyl ester of N-Nitro-N-n-butylcarbamic acid	(15.)	below-70°C	1.1055
6. Ethyl ester of N-Nitro-N-secbutylcarbamic a	cid (15.)	below-70°C	1.094
7. Methyl ester of N-Nitro-N-isobutylcarbamic aci	d (15.)	2°C	1.144
8. Ethyl ester of N-Nitro-N-isobutylcarbamic aci	d (15.)	below-75°C	1.101
9. Ethyl ester of N-Nitro-N-n-hexylcarbamic acid	(15.)	-60° C	1.062
10. Methyl ester of N-Nitro-N-methylcarbamic acid	(3.) 158°C		1.065
ll. Methyl ester of N-Nitro-N-ethylcarbamic acid (3.) 165°C		1.019

The compounds listed in Table I were prepared mainly for the synthesis of nitroamines. The general method of preparing nitroamines by ammonolysis of the corresponding nitrourethans is given by Thomas (12.).

The nitrourethan was dissolved in ether and a current of dry ammonia was passed into the solution. The ammonium salt of the nitroamine precipitated as a mass of crystals, which were filtered and washed with ether.

The compound of ammonia with the nitroamine separated as a gelatinous mass which absorbed much ether and was consequently very difficult to purify. Replacing ether with either chloroform or benzene gave no better results.

The ammonium salt of the nitroamine was then decomposed with dilute sulfuric acid and the nitroamine was extracted with ether.

Evaporation of the ether yielded pure nitroamines as shown by analysis.

Sp.gr. 0 15°C	F.E.	B.P.	Diabal	100
1,1055	Dolow-TOOG		Sthyl ester of N-Nitro-N-n-butylcarbamic acid (15.)	5.
1.094	pelow-700c		Ithyl ester of W-Mitro-N-secbutylcarbamic soid (15.	. 8
1.144			le rejse lydjell (15.) N-Mitro-W-inobutylosrbamic acid (15.)	7.
1.101	below-75°C		Ethyl seter of N-Witro-W-isobutylearbamic soid (15.)	.8
1.062	0°08~		Ethyl ester of N-Mitro-N-m-hexylcerbemic sold (15.)	. e
1.065		158°C	Methyl seter of M-Nitro-W-mathylcerbamic sold (5.)	10.
1.019		165°C	Methyl ester of N-Nitro-N-ethyloarbamic acid (3.)	II.

The compounds listed in Table I were prepared mainly for the synthesis of nitrosmines. The general method of preparing nitrosmines by smanonolysis of the corresponding nitrosmethans is given by Thomas (12.).

The nitrourethems was dissolved in ether and a current of dry emissions was passed into the solution. The ammonium salt of the nitrosmine precipitated as a mass of crystals, which were filtered and washed with ether.

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The same and the nitrosmine was then decomposed with there.

Allows as the state was entrosmine was extracted with other.

Evaporation of the other yielded ours nitrosmines as shown by analysis.

The nitroamines prepared by this method and their physical properties are listed in Table II.

TABLE II

PROPERTIES OF NITROAMINES

COMPOUND B.P. F.P. Sp.g	gr.@ 15°C
1. N-Nitromethylamine (1.) 38°C	erives two
2. N-Nitroethylamine (14.)	1.1675
3. N-Nitro-n-propylamine(12.) 128°-129°C @ 40mm.	1.102
4. N-Nitro-isopropylamine (12.) 90°-91°C @ 10mm4°C	1.098
5. N-Nitro-n-butylamine (15.)	1.0665
6. N-Nitro-secbutylamine (15.) -34.5°C	1.066
7. N-Nitroisobutylamine (15.) 32.2°C	
8. N-Nitro-n-hexylamine (15.) 5.5 to 6.5°C	1.014

A great deal of work has been done with the nitroamines, especially in relation to alkyl derivatives and metallic salts of these compounds.

Since one of the objects of this thesis is to characterize the hydrolysis products of nitrourethans a brief discussion of the chemistry of the nitroamines will not be out of place at this point.

Van Erp (15.) prepared the potassium salt of N-Nitro-N-n-butyl amine by mixing alcoholic solutions of the nitroamine and potassium hydroxide in equivalent quantities.

$$n-C_4H_9-NH-NO_2 \neq KOH \longrightarrow \left[n-C_4H_9-N-NO_2\right] K^+ \neq HOH$$

In this same paper Van Erp (15.) describes the preparation of the methyl derivative of n-butylnitroamine from equivalent quantities of the potassium salt of the nitroamine and methyl iodide in methanol solution.

$$\begin{bmatrix} n-C_4H_9-N-NO_2 \end{bmatrix}^- K^+ \neq CH_3I \longrightarrow (n-C_4H_9)(CH_3)N-NO_2 \neq KI$$

The nitroswines prepared by this method and their physical properties are listed in Table II.

PROPERTIES OF NITEGAMENCS

59.gr.@ 15°C	1.7.2	B.P.		COMPOUND
	3800	6	.1) enimalyntem	1. M-Nitro
1.1675	909	(ethylemine (14.	2. N-Witro
1,102		12.) 1280-1290 c 40mm.	-n-cropylemine(3. N-Nitro
1.098	5° A.	(18.) 90°-91°c @ 10mm.	· isopropylemine	4. W-Witro
1.0665	-5° to /5°c	15.)) enimalyjud-a-	5. NeMitro
1.066	24.5°C	(15.)	seebutylemin	6. N-Nitro
	32.2°g	15.)) enlesityledes	77 Nellitro
1.014	5.5 to 6.5°C	15.)) enimalyxad-n-	e-niin-M .8

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Van Erp (15.) prepared the potassium salt of N-Nitro-N-n-butyl amine by mixing alcoholic solutions of the nitrosmine and potassium by-droxide in equivalent quantities.

ent to noitereque ent sediroseb (.21) que may reque emas sint mi entro selitios of the methyl derivativa of nebutylnitrosmine end methyl iodide in methanol solution.

b

The work of Van Erp described above provoked a series of investigations on metallic and alkyl derivatives of nitroamines by Franchimont and his collaborators (4, 5, 13, 14). The potassium salts of ethyl and propylnitroamine were prepared and other metallic derivatives were obtained from them by reaction with various metallic salts. The sodium derivative was obtained by reaction with alcoholic sodium hydroxide, the lithium derivative from alcoholic lithium carbonate and the silver derivative from alcoholic silver nitrate.

The dialkyl nitroamines, prepared by these investigators by the reaction of an alkyl iodide with the sodium or potassium salt of a nitroamine, are summarized in the following table.

TABLE III
PROPERTIES OF DIALKYLNITROAMINES

COMPOUND	B. P.	Sp.gr. @ 15°C
1. N-Nitromethylethylamine (14.)	90.5°C @ 23mm.	1.1012
2. N-Nitrodiethylamine (14.)	96°C @ 18mm.	1.057
3. N-Nitro-n-propylethylamine (13.)	108°C @ 22mm.	1.028
4. N-Nitroisopropylethylamine (13.)	65°C @ 20mm.	.9783
5. N-Nitroisopropylmethylemine (13.)	51°C @ 18mm.	1.012
6. N-Nitroallylmethylamine (4.)	96°C @ 18mm.	1.1015
7. N-Nitrooctylmethylamine (5.)	164.5°C @ 17.5mm.	.965
8. N-Nitro-n-butylmethylamine (1.)		1.0268
9. N-Nitroisobutylmethylamine (1.)	104°C @ 17mm.	

B. Present Work

The foregoing historical survey of the literature reveals that a great deal of constructive work is yet to be done on the alighatic

The work of Yen Erp described above provoked a sories of investigation on metallic and skyl derivatives of nitrosmines by Franchimont and his collaborators (4, 5, 13, 14). The potential selts of athyl and propylationalise were prepared and other metallic derivatives were obtained from them by reaction with verious metallic selts. The sodium derivative was obtained by reaction with alcoholic sodium hydroxids, the lithium derivative from sicoholic lithium carbonate and the silver derivative from sicoholic silver nitrate.

The dislay nitrosmines, prepared by these investigators by the restion of an alive lodide with the modium or potential of a nitrosmine, are summarized in the following table.

TABLE ITE

8p.gr. 3 15 od	B. P.	COMPOUND
1.1012	90.5°C @ 23mm.	1. N-Nitromethylethylemine (14.)
1.057	96°C @ 18mm.	2. N-Nitrodistnylamins (14.)
1,028	108°C @ 22mm.	8. M-Mitro-a-propylethylamine (13.)
,9783	65°C @ 20mm.	4. N-Nitroisogropylethylenine (13.)
1.012	51°C @ 18mm.	5. N-Witroleogropylmethylemine (13.)
1,1015	96°C @ 18mm.	(.t) eninslydemiylisorin-M .8
.365	164,5°C @ 17.5mm.	7. N-Nitrocctylmethylamine (5.)
1,0268		(.1) enimslyddemlydud-n-ordlW-W .8
	104°C @ 17mm.	9. N-Mitroteobutylmethylamine (1.)

B. Fresent Work

The foregoing historical survey of the literature reveals that a great lead of constructive work is yet to be done on the sliphatic

nitroamines and nitrourethans. The problem of the present work consists essentially of an attempt to determine the resistance of the nitrourethans to hydrolysis in acidic and basic media and the concentrations of these reagents necessary to effect complete hydrolysis in a particular interval of time. The mechanism of the hydrolysis and the products of the hydrolysis were to be investigated and the reaction products were to be characterized in the event that any unfamiliar products were obtained. The experiments described below were confined sclely to one member of the nitrourethan series, N-Nitroisopropylurethan.

Base catalyzed hydrolysis was expected to conform to the following electronic interpretation. The first step involves attachment of the hydroxyl group to the carbonyl carbon atom.

1.
$$R-N:C:O:C_2H_5 \neq :O:H \longrightarrow \begin{bmatrix} NO_2:O:\\ R:N:C:O:C_2H_5 \end{bmatrix}$$

The resulting negative ion then reacts with the water in the reaction medium.

2.
$$\begin{bmatrix} NO_2 : 0: \\ R: N : C : 0: C_2H_5 \end{bmatrix} \neq H: 0: H \longrightarrow R: N : C \Rightarrow C_2H_5 : 0: H \neq : 0: H$$

$$: 0: H$$

Thus we see that the molecule is split and the catalyst is regenerated.

The last step involves decomposition of the unstable carbamic acid type of compound to yield carbon dioxide and a nitroamine.

NO₂ :0 NO₂
R:N: C:O:H
$$\rightarrow$$
 R-N-H \neq CO₂

If hydrolysis is effected in an acid medium, there are two points in the nitrourethan molecule which might be attacked by the reagent. The carbonyl oxygen atom can assume a negative charge through resonance.

nitrosmines and nitrovruthens. The problem of the present work consists of time. The mechanism of the hydrolysis and the products of the hydrolysis series, M-Witroisogrouylurethan,

Base catalyzed hydrolysis was expected to conform to the following

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Thus we see that the molecule is split and the cetalyst is regenerated. To egyf blos pimed rep eldafanu wit To nolfisogmoneb sevlevni gefe fasl edT compound to yield corbon dioxide and a nitroamine.

If hydrolysis is effected in an acid medium, there are two points in the mitrourethen molecule which might be sitessed by the researt. carbonyl oxygen atom can assume a negative charge through resonance.

NO2 :0:

NO2 :0:

R-M-C:0:Rl

If hydrolysis actually followed a path similar to that of ester hydrolysis, the mechanism would be as follows.

The first step would involve the attack of a proton upon the carbonyl oxygen atom.

The resulting positive ion can then react with a molecule of water, decomposing the ion and regenerating the catalyst.

2.
$$R-N-G-OR^1 \neq H:O:H \longrightarrow R-N-G-OF \neq R^1OH \neq H^+$$

Again the unstable carbamic acid derivative should decompose to give the nitroamine and carbon dioxide.

3.
$$R-N$$
 $-C$ OH \longrightarrow $R-N$ H $+$ CO_2

The second possible point of attack is the amino nitrogen atom.

The proton presumably can attach itself to the unshared electron pair at this point.

1.
$$R-N:C:O:C_2H_5 \neq H$$

Respectively.

Respective

This positive ion can then react with a water molecule as follows.

2.
$$\begin{bmatrix} NO_2 \\ R-N : C : O : C_2H_5 \end{bmatrix} \neq H : O : H \longrightarrow \begin{bmatrix} NO_2 \\ R-N : C : O : H \end{bmatrix} \neq H : O : C_2H_5$$

The resulting cerbamic acid type of compound will then decompose to yield the nitroamine and carbon dioxide and to regenerate the catalyst.

3.
$$\begin{bmatrix} NO_2 \\ R-N:C:O:H \end{bmatrix}^+ \longrightarrow R-N \xrightarrow{NO_2} CO_2 \neq H^+$$

There is, however, a possibility that hydrolysis cannot proceed by this second postulated mechanism because the unshared pair of electrons can resonate with the nitro group thus decreasing the availability of this unshared pair to attack by the proton.

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The resulting positive ion can then react with a molecule of water, decommosing the ion and regenerating the datalyst.

Again the unstable cerbamic sold derivative should decompose to give the

The second possible point of stack is the anished bucker of the unshand electron pair at this point.

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There is, however, a possibility that hydrolysis cannot crossed by this escond postulated rechanism because the unshared pair of electrons can resonate with the nitro group thus decressing the availability of this unshared pair to attend by the cross of the cross o

Structures of this type, especially since some of them place a negative charge on the carbonyl oxygen atom, a requisite for proton attachment in the first postulated mechanism, make it seem rather doubtful that hydrolysis proceeds by this second mechanism.

Reasoning on the basis of the second mechanism certain electrophilic reagents and reagents capable of forming a hydrogen bond with the
unshared pair were to be added to the hydrolysis mixtures to determine
whether or not hydrolysis could be inhibited or prevented by their presence.

It was also postulated that hydrolysis could not be prevented by these particular reagents in alkaline media, not only because of the intability of electrophilic reagents to maintain the open sextet in basic solution which is necessary for attachment of the inhibitor to the unshared electron pair; but also hydrolysis was expected to proceed by a different path under alkaline conditions.

The results of this and similar investigations designed to determine the true mechanism are discussed subsequently.

The methods employed for the experimental work described below were the standard procedures of quantitative chamistry and the preparative techniques of the organic chemist.

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Passoning on the basis of the second mechanism negligible of the spinite respents and respents cample of forming a hydrogen bond with the unshered pair were to be added to the hydrolysis mixtures to determine whether or not hydrolysis could be included or prevented by their presents.

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actic under alkaling conditions.

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II PREPARATION OF NITROURETHANS:

Nitrourethans were first investigated and employed for the synthesis of nitroamines by Franchimont and Klobbie (3.). Their method of preparation as revised by Thomas (12.) is described briefly in the following paragraphs.

Either ethyl or methyl chloroformate was cooled in an ice bath and a 25% aqueous solution of the amine was added slowly. The product was extracted with ether and the ethereal solution was dried and fractionally distilled. The urethans obtained in this manner were nitrated as follows: The urethans were added drop by drop to 3 or 4 molecular equivalents of nitric acid, keeping the temperature at about 0°C. The nitric acid solution was then poured onto crystals of sodium carbonate which were covered with a little water and the whole mixture was cooled. A yellowish liquid separated and was extracted with ether. The ether was distilled and the residue was dried by extraction with sulfuric acid.

The isopropyl nitrourethan used in this research was prepared by the same basic procedure as that outlined above but many improvements have been added.

A two-liter three-necked flask was used, equipped with a 500 c.c. dropping funnel, a mechanical stirrer and a thermometer. The compound used in these researches was always prepared in batches of the following size: Three moles of sodium hydroxide were dissolved in 180-210 c.c. of wwater in the two-liter flask and the flask was cooled in an ice-bath. Three moles of isopropylamine in 90 c.c. of water were added slowly with stirring, keeping the temperature of the reaction mixture at about 0°C. Then three moles of ethylchlorocarbonate were added through the dropping

II PREPARATION OF MITSCOURSTHAMS

Mitrour Strans were first investigated and employed for the synthesis of mitrosmines by Franchisom and Michbele (3.). Their method of preparation as revised by Thomas (12.) is described briefly in the following paragraphs.

Fither sthyl or metnyl chloroforents was cooled in an ice bath

and a 25% equeous solution of the smine was added slowly. The product was attracted with ather and the etherest solution was dried and fractionally distilled. The unsthans octained in this menner were mitrated as follows: The unsthans were added drop by drop to 3 or 4 molecular equivalents of mitric soid, keeping the temperature at about 0°C. The mitric acid solution was then poured onto mystale of sodium carbonate which were covered with a little water and the whole mixture was cooled. A yellowish liquid separated and was extracted with ether. The ether was distilled and the residue was dried by extraction with eatherts acid.

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funnel at such a rate that the temperature did not rise above 15°C. A 5% excess of the amine was used. After complete addition of the ethyl chlorocarbonate (about 2 hours), stirring was continued for about fifteen minutes. Then the mixture was placed in a separatory funnel and the bottom layer was drawn off. The top layer was dried with the least possible quantity of potassium carbonate so that it appeared clear, not turbid. The isopropylurethan was then distilled under reduced pressure using a water pump (B.P. 64°C @ 7mm). The low boiling fraction was isopropylamine.

1.
$$CH_3$$
- CH_2 OC-C1, M.W. = 109, 3 x 109 = 327gr.

2.
$$(CH_3)_2$$
-CH-NH₂, M.W. = 60, 3 x 60 = 180gr.

5% excess (180) (105/100) = 189 189gr.

3. NaOH,
$$M.W. = 40$$
. $3 \times 40 = 120$

Assuming that the NaOH is 90% pure: (120) (100/90) = 133

For safety a 10% excess is used: (133) (110/100) = 147 147gr.

Function of the sodium hydroxide:

The reaction may be carried out in the absence of base but under such conditions two moles of amine are required to react with one mole of the ethyl chlorocarbonate. The first mole of the amine would then react with the ethylchlorocarbonate to form the urethan and the second mole would react with the hydrogen chloride produced by the first reaction to yield the amine hydrochloride.

$$(GH_3)_2GH-NH_2 \neq HG1 \longrightarrow (GH_3)_2GH-NH_2-HG1$$

formed at such a rate that the temperature did not rise above 15°C. A 5% excess of the amine was used. After complete addition of the ethyl chierocarbonate (about 2 hours), stirring was continued for about fifteen minutes. Then the mixture was placed in a separatory funnel and the botton layer was drawn off. The top layer was dried with the least possible quantity of potassium carbonate so that it appeared clear, not turbid. The isopropylurathen was then distilled under reduced pressure using a water pump (g.r. 5400 @ 7mm). The low boiling fraction was icopropylamine.

The resotion proceeds as shown by the following equation.

Option of the resotion proceeds as shown by the following equation.

Option of the process of the the sample of the this preparation were based on the following calculations:

1. cH3-cH2od-c1, N.W. = 109, 3 x 109 = 327gr.

2. (CHg) 2-CH-NH2. M.W. = 60. 3 x 60 = 180gr.

5% excess (180) (105/100) = 189 189gr.

3. NaOH, 3. NaOH, 3 x 40 = 180

Assuming that the MaOH is 90% ours: (120) (100/90) = 133
For safety a 10% excess is used: (133) (110/100) = 147 147gr.

Function of the sodium hydroxide:

The reaction may be carried out in the absence of base but under such conditions two moles of emine are required to react with one mole of the ethyl chlorocarbonate. The first mole of the emine would then react with the ethylchlorocarbonate to form the arethen and the second mole would react with the hydrogen chloride produced by the first reaction to yield the emine hydrochloride.

(CH3) 2CH-NH2 / HCI ----> (CH3) 2CH-NH2-HCI

The use of the sodium hydroxide is to neutralize this HCl as repidly as it is formed so that the amine may remain free for reaction with the ethylchlorocarbonate.

Nitration of the isopropylurethan:

The method of Franchimont and Klobbie (3.) required three or four times the theoretical amount of nitric acid if nitration was to be effected satisfactorily, the main reason being that the water produced in the reaction so diluted the nitric acid when only one molecular equivalent was used that its efficiency as a nitrating agent was greatly impaired. The following procedure utilizes acetic anhydride as a means of removing this water of of reaction.

The overall reaction proceeds as follows.

 $(CH_3)_2$ -CH-NH-C-0-C₂H₅/HONO₂/ $(CH_3CO)_2O$ \longrightarrow $(CH_3)_2$ -CH-N(NO₂)-C-0-C₂H₅/2CH₃COOH This procedure was carried out on all of the product obtained in the previous discussion. The quantities of reagents employed will be discussed later.

Fuming nitric acid (white) was added through a dropping funnel to the acetic anhydride which was enclosed in a two-liter, three-necked flask which was equipped with a thermometer and a mechanical stirrer. The flask was cooled in an ice-salt mixture and during the addition of the nitric acid the temperature was not allowed to rise above 10°C, keeping it most of the time between 5°-8°C. After the nitric acid was added, the ice bath was replaced by a water bath at approximately 18°C. The urethan was then added at such a rate that the temperature remained below 35°C. After all of the urethan had been added, stirring was continued for ten minutes.

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The reaction mixture was poured into a volume of water which was about three times its own volume. The nitrourethan was the bottom layer. The nitrourethan was separated and washed repeatedly with dilute potassium carbonate solution until free from acid. It was washed with water and dried by filtering through two or three pieces of filter paper. It was then distilled under reduced pressure using an electric pump.

 $(B.P. 72^{\circ} @ 7mm) (MD = 1.4381).$

Discussion of Quantities used:

- 1. Enough acetic anhydride must be used to react with all of the water in the nitric acid and all of the water formed in the reaction.
- The acetic anhydride used was assumed to be 90% pure. The calculations were based on this and a 5% excess was used for safety.
- 3. The fuming nitric acid used was 87% HNO3.
- 4. For rapidity and safety a 50% excess of nitric acid was used.

Calculations:

 HNO_3 , M.W. = 63, 3 moles = 3x63 = 189 gr.

HNO3 (fuming) is 87% HNO3

Therefore the weight of solution necessary to insure the presence of three moles of HNO3 is:

$$(189)(100/87) = 217$$
 grams.

It is intended, however to use a 50% excess of HNO3, since a 50% excess is necessary for a complete nitration.

(217) (1.50) = 325 grams.

Weight of water in 325 grams of fuming nitric acid:

Since we have 87% HNO2 we must have 13% H2O.

(325) (.13) = 42.3 grams of water

The resustion mixture was poured into a volume of weter which was ebout three times its own volume. The mitrour sthan was the bottom layer. guiresto etulib ntiv ylbetsecen bedesw bna betsnose sew nedferwordin edT esw iT . ress neglif to seeig cerns to owt depend gainetlin yd beinbt

(B.P. 720 @ 7mm) (Mg = 1.4381).

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- 2. The acetic ambydride used was assumed to be 90 pure. The calculations
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Since we have SYL HWO we must heve 13t Hoo.

refew lo smarg 8.54 = (81.) (888)

Moles of water in nitric acid used:

(42.3/18) = 2.35 moles.

Water of Reaction:

 $(CH_3)_2$ -CH-NH-COOC₂H₅ \neq HONO₂ \longrightarrow $(CH_3)_2$ -CH-N(NO₂)-COOC₂H₅ \neq H₂O

If three moles of urethan react, three moles of water will be formed.

Total moles of water requiring removal:

 $3 \neq 2.35 = 5.35$ moles H_{20}

Acetic Anhydride:

One mole of acetic anhydride reacts with one mole of water.

(CH₃CO)₂O ≠ H₂O → 2CH₃COOH

M.W. = 102. 1 mole = 102 grams.

Weight of Acetic Anhydride necessary to react with all water.

(102) (5.35) = 546 grams.

Since this is assumed to be only 90% (CH3CO)20 we use:

(546)(100/90) = 606 grams.

For safety a 5% excess of (CH3CO)2O should be used.

(606) (105/100) = 636 grams

Summary

To nitrate three moles of isopropylurethan:

393 gr. isopropylurethan

325 gr. fuming nitric acid

636 gr. acetic anhydride

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(48.3/18) = 2.35 moles.

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(CH3)2-CH-NH-COOC2H5 + HONO2 -- (CH3)2-CH-N(NO2)-COOC2H5 + H2O

of three moles of water required, three moles of water will be formed.

3 / 2.35 = 5.35 moles HgO

Agetic Ambydride:

. retsw lo elor eno ditw escer abirbydna oligeos lo elor eno

M.W. = 102, 1 mole = 108 grams.

. weight of Acetic Anhydride mecessary to resol to inglew

(102) (5.35) = 546 grams.

Since this is samuad to be only 90% (CH200)20 we use:

(546) (100/90) = 506 grams.

For sefety a 5% excess of (CHgCO)gO should be used.

(606) (105/100) = 636 grama

Summary

To nitrate three moles of leopropylurethen:

393 gr. isograpylurethen

325 gr. fuming nitric sold

636 gr. scable amiyarida

III BASIC HYDROLYSIS

A. Introduction

The classical method of decomposing a nitrourethan was to run dry ammonia into its ethereal solution and to decompose the precipitated ammonium salt with dilute sulfuric acid (3.). Details of this process are discussed in the introductory section of this paper.

The reaction proceeds as follows:

$$R-N(NO_2)-COOC_2H_5 \neq 2NH_3 \longrightarrow R-N(NO_2)(NH_4) \neq NH_2-COOC_2H_5$$

Search of the literature, however, revealed no attempts at bringing about a similar reaction by means of hydrolysis. On the basis of the
above equation it seemed logical to conclude that hydrolysis would take
place in the following manner:

$$R-N(NO_2)-COOC_2H_5 \neq HOH \longrightarrow R-NH-NO_2 \neq HO-COOC_2H_5$$

 $HO-COO-C_2H_5 \longrightarrow C_2H_5OH \neq CO_2$

Since there was no evidence of experimentation along this line by previous investigators, instigation of a program of research along these lines appeared to be desirable.

The procedure used for the hydrolysis of N-Nitroisopropylurethan and determination of percentage hydrolysis is relatively simple and worked well from the very first.

The compound was hydrolyzed by refluxing it for certain definite periods of time with sodium hydroxide of varying concentrations. It was predicted that the nitrourethan would hydrolyze in such a way that for every mole of urethan hydrolyzed, a mole of carbon dioxide would be produced.

 $(CH_3)_2$ -CH-N(NO₂)-COC₂H₅ / HOH \longrightarrow $(CH_3)_2$ -CH-NH-(NO₂) / CO_2 /C₂H₅OH The carbon dioxide would of course react with the alkaline medium thusly:

$$CO_2 \neq 2NaOH \longrightarrow Na_2CO_3 \neq H_2O$$

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The work of Thomas (12.) suggested that probably the resulting nitroamine would be converted into its sodium salt.

$$(CH_3)_2CH-NH-NO_2 \neq NaOH \longrightarrow (CH_3)-CH-NNa-NO_2 \neq H_2O$$

The hydrolysis mixtures were then transferred quantitatively to volumetric flasks. Aliquot portions were then taken and titrated to the phenolphthalein end-point with dilute HCl. The following two reactions were expected.

NaOH
$$\neq$$
 HCl \longrightarrow NaCl \neq H₂O
Na₂CO₃ \neq HCl \longrightarrow NaHCO₃ \neq NaCl

The titration was then continued to the methyl orange end-point during which time the following reaction was expected to take place.

$$NaHCO_3 \neq HC1 \longrightarrow NaC1 \neq CO_2 \neq H_2O$$

In this manner it was proposed to determine the percentage hydrolysis by quantitative titration of the carbon dioxide evolved in the reaction.

However, basing the calculations for some of the earlier runs on the above equations alone, gave results in the vicinity of 200% hydrolysis.

If we consider the products of the reaction, however, we find that the isopropylnitroamine can form a sodium derivative which cannot exist in acid solution. For every molecule of carbon dioxide formed by hydrolysis of the nitrourethan, a molecule of the nitroamine is also formed. The nitroamine would then form its sodium derivative very rapidly.

 $(CH_3)_2CH-NH-NO_2 \neq NaOH \longrightarrow (CH_3)_2CH-NNa-NO_2 \neq H_2O$ If we assume that the sodium derivative is present at the phenolphthalein end point and is decomposed completely only at the methyl orange end point, it is obvious that we have the following two reactions contributing to the titration.

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(CH₃)₂CH-NH-NO₂ ≠ NaOH ——— (CH₃)₂CH-NNa-NO₂ ≠ H₂O

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 $NaHCO_3 \neq HC1 \longrightarrow NaC1 \neq CO_2 \neq H_2O$

 $(CH_3)_2CH-NNa-NO_2 \neq HC1 \longrightarrow (CH_3)_2CH-NH-NO_2 \neq NaC1$ Thus it is shown that two equivalents of hydrochloric acid are necessary for every equivalent of nitrourethan hydrolyzed. It is clear that hydrolysis of the nitrourethan in basic medium proceeds as follows: $(CH_3)_2-CH-N(NO_2)-COOC_2H_5 \neq 3NaOH \longrightarrow (CH_3)_2-CH-NNa-NO_2 \neq Na_2CO_3 \neq C_2H_5OH \neq H_2O$ and that three moles of sodium hydroxide are required for every mole of nitrourethan.

On the basis of the above reasoning, runs in which hydrolysis was obviously complete gave 100% hydrolysis rather than 200% upon application of the appropriate calculations.

When the isopropylnitroamine was finally isolated (see below) it was found that its water solutions were acidic to litmus and that quite a few drops of 10% NaOH solution were necessary to bring out the red color of the phenolphthalein.

B. General method of Investigation:

The hydrolyses in basic media were all carried out in this manner:

A 500 c.c. round bottomed flask equipped with a long reflux condenser was
used as a reaction vessel. One-hundred cubic centimeters of sodium hydroxide
solution of the desired concentration were pipetted into this flask and a
small quantity of isopropylnitrourethan was weighed into the flask from a
small dropping bottle. A boiling chip was added and the mixture was refluxed for the desired length of time. The mixture was then allowed to
cool and transferred quantitatively to a 200 c.c. volumetric flask and
diluted to volume. Aliquot portions (50 c.c.) were then titrated with
dilute hydrochloric acid to the phenolphthalein end point.

NAHCO3 + HCL ---- NaCT + CO2 + H2O

Thus it is shown that two squivelents of hydrochloric acid are necessary -yd tedt meels at II. besylorbyd medicuratin to theleviupe yreve rol trouvelet as absecon multem pland ni medicuratin ad to slaylorb.

(CH3)2-CH-N(NO2)-COC2H5/3NaCH --- (CH3)2-CH-NNA-NO2/Na2CO3/C2H5OH/H2O
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solution of the desired concentration were pipetted into this flask and a
small quantity of isopropylnitrourethen was weighed into the flask from a
small dropting bottle. A boiling only was added and the mixture was refluxed for the desired length of time. The mixture was then allowed to
cool and transferred quantitatively to a 200 c.c. volumetric flask and
diluted to volume. Aliquot portions (50 c.c.) were then titrated with

From this point on the titration was continued with standard hydrochloric acid (approximately .4N) standardized against standard sodium carbonate.

Appropriate blanks were run from a solution containing 100 c.c. of the NaOH solution and 100 c.c. of water. The percentage hydrolysis was calculated from the type of data shown below:

C. Sample Calculation:

Basic Hydrolysis of N-Nitroisopropylurethan (5% NaOH)

(4 hours refluxing, 100 c.c. of 5% NaOH)

 Wt. bottle and sample
 47.8219

 Wt. bottle
 37.4822

Wt. sample 10.3397

The molecular weight of N-Nitro isopropylurethan is 176, while that of GO_2 is 44. 176/44=4. The factor, 4, is used to obtain the weight of GO_2 possible to observe by dividing it into the weight of the sample. Thus, theoretical GO_2 10.3397/4=2.5849 gr.

Moles CO_2 : 2.5849/44 = .05875 = 58.75 millimoles In a 50 c.c. aliquot there will be: 58.75/4 = 1469 millimoles

TITRATIONS

	I			II	
End	49.23		1.02	End	49.60
Start	58		28	Start	25
Total	48.65	+	.74	Total	49.35
Total	49.39				

Volume of HCl necessary for the blank = .60 c.c.
Average titrated volume 49.37 c.c.

49.37 - .60 = 48.77 c.c.

From this point on the titracion was continued with standard hydrochloric edid (a proximately .4N) standardized against standard sodium carbonate.

Approximate blanks were run from a solution containing 100 c.c. of the NaCH solution and 100 c.c. of water. The percentage hydrolysis was calculated from the type of data shown below:

n. Sample Calculation:

Resid Hydrolysis of N-Mitrolsopropylarstnan (5% MaOH)

Wt. bottle and sample 47,8219

17. bottle 37.4822

Wt. sample 10.3397

The molecular weight of N-Mitro isograpylurathen is 176, while that of CO2 is 44. 176/44=4. The factor, 4, is used to obtain the weight of CO2 possible to observe by dividing it into the weight of the sample. Thus, theoretical CO2 10.3397/4=2.5849 gr.

The 50 c.c. aliquet there will be: 56.75/4 = 1459 millimoles

TITHAT TONS

	II			
49.60		50.1	49,23	
88.	stort	.28	.58	Start
49.35	LefoT	49.	48.65	LetoT
			49.39	fatoT

Volume of HCl messessry for the blank = .60 c.c.
Average titrated volume 49.37 c.c.

49.37 - .60 = 48.77 6.6.

If the hydrolysis were complete 14.7 millimoles of $^{\rm CO}_2$ would be titrated, but since we have an equivalent amount of nitroamine formed, the total titration should run to 2x14.7 = 29.4 millimoles:

The HCl used had a normality of .4531

(.4531) (48.77) = 22.1 millimoles

Thus:

Percentage Hydrolysis (4 hrs.) (100)(22.1)/29.4 75.2%

The results obtained by this method are tabulated below:

TABLE IV

PERCENTAGE HYDROLYSIS IN BASIC MEDIUM

% NaOH	Volume	Time	% Hydrolysis
10%	100 c.c.	4 hrs.	96.4%
10%	100 c.c.	4 hrs.	98.3%
10%	100 c.c.	3 hrs.	99.1%
10%	100 c.c.	2 hrs.	95.4%
20%	100 c.c.	4 hrs.	94.3%
5%	100 c.c.	4 hrs.	75.2%
5%	150 c.c.	6 hrs.	97.2%
3%	100 c.c.	4 hrs.	54.7%
1%	100 c.c.	4 hrs.	31.5%

In the case of the one percent hydrolysis tabulated above, the mixture was neutral to both litmus and phenolphthalein at the end of the refluxing.

The value 31.5% was obtained by titration directly to the methyl orange end point.

D. Further Hydrolysis:

It was thought at the initiation of this investigation that

to the hydrolysis were complete 14.7 millimoles of CO2 would be titrated, but since we have an equivalent amount of mitronmine formed, the total titration should run to 2x14.7 = 29.4 millimoles:

The HCl used had a normality of .453l

selomillim 1.58 = (77.84) (1884.)

Thus:

Percentage Hydrolysis (& hrs.) (100)(22.1)/29.4 75.2/ The results obtained by this method are tabulated below:

TABLE IV. BASTI MEDIUM

& Hydrolysia	enlT	emuloy	HOAN >
36.45	.end &	100 c.c.	
98.3%	4 hrs.	100 0.0.	10%
99.1%	3 hrs.	100 0.0.	
95.4%	2 hrs.	100 0.0.	
94.3%	4 hrs.	100 0.0.	
75.24	.and 4	100 c.c.	5%
75.76	.ami å	150 c.c.	
34,75	-and -	100 0.0.	
la.is	4 hra.	100 0.0.	

In the case of the one percent hydrolysis tabulated above, the mixture was neutral to both litmus and phenolphthalela at the and of the refluxing.

The value 81.5° was obtained by titration directly to the mathyl orange and coint.

D. Further Hydrolysis:

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further hydrolysis might occur to yield isopropyl amine and nitric acid according to the following equation.

 $(CH_3)_2$ -CH-NH-NO₂ \neq HOH \longrightarrow $(CH_3)_2$ -CH-NH₂ \neq HONO₂

The amine if liberated would undoubtedly escape as vapor from the hot alkaline solution.

Its presence could not be detected by smell and moistened piece of red lutmus paper fastened to the top of the condenser did not change color throughout the refluxing even when 20% NaOH was employed. Attempts to get a brown ring test with ferrous sulfate solution and concentrated sulfuric acid on the reaction mixture were futile. We may therefore conclude that, at least in the hydrolysis media employed, the nitrogram does not hydrolyze.

prospers. It is evidently 97.00 pure.

3. Addition of Excess Alkali and Back Titration with NYL

water and an aware of standard wheal may added as the characteristical

and-point was definitely past. The mixture was then ditrated to both th

phenolphthelpin and the methyl armage and points with standard NCL.

.0300/104 = .00789 uelss of mitrosules

Total volume of base sided 44.54 c.c. (.2500)

(46.86) (.860) = 11.67 m.w. Nach

Values of soid to reach chesnighthalain and point 23,56 s.v.(.1169

(33.86) (116) ± 3.92 m, a,

further hydrolysis might occur to yield isogropyl smine and nitric sold according to the following squation.

(CH₃)₂-CH-NH-NO₂ / HOH - (CH₃)₂-CH-NH₂ / HONO₂
The smine if liberated would undoubtedly escape as vapor from the hot

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E. Evidence for Correctness of Analytical Procedure

1. Neutral Equivalent of Isopropylnitroamine

A weighed sample of isopropylnitroamine was dissolved in 50 c.c. of distilled water and titrated to the phenolphthalein end point with standard sodium hydroxide solution.

Weight of sample:

.8205 gr.

Volume of NaOH:

29.34 c.c.

Normality of NaOH:

.260

Molecular Weight

104

.8205/104 = .00790 moles of nitroamine

(29.34) (.260) = .00765 moles of NaOH

(100) (.00765)/(.00790) = 97.0% pure.

The nitroamine employed was extracted from the reaction mixture with ether, the ether distilled on a steam bath and the residue distilled under reduced pressure. It is evidently 97.0% pure.

2. Addition of Excess Alkali and Back Titration with HCl

A weighed sample of the nitroamine was dissolved in 50 c.c. of water and an excess of standard alkali was added so the phenolphthalein end-point was definitely past. The mixture was then titrated to both the phenolphthalein and the methyl orange end points with standard HCl.

Weight of sample: .8200 gr.

.8200/104 = .00789 moles of nitroamine

Total volume of base added 44.84 c.c. (.260N)

(44.84) (.260) = 11.67 m.e. NaOH

Volume of acid to reach phenolphthalein end point 33.86 c.c.(.116N)

(33.86) (.116) = 3.92 m.e.

E. Evidence for Correctness of Analytical Rosedure.

1. Meutral Equivalent of Isomopyinitrosmins

A weighed sample of isographinitrosmine was dissolved in 50 c.c.

diff with said the phonological and point with

standard sodium hydroxide solution.

.8205 kg.

resques to disjew.

.0.0 AE. ES

:HOSM to emuloV

nae

Normality of NaOH:

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emimacriin lo melom 00700. = 401\8088.

HOM lo melow coron = (008.) (48.98)

(100) (.00765)/(.00790) = 97.0% pure.

The nitrosmine employed was extracted from the restrict mixture with ether. because reduced the clistified under reduced the content of the state of the content of the con

2. Addition of Excess Alkali and Esch Titration with HOL

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(44.84) (.860) = 11.67 m.s. NaOH

(Wall.).o.o 38.88 sning bne misled the month of the sound of the state of the sound of the state of the state

(33.86) (.116) = 3.92 m.e.

Millequivalents of Base Neutralized by Nitreamine:

11.67-3.92 = 7.75 = .00775 moles.

Percentage Purity of the Nitroamine:

(100) (.00775)/(.00789) = 98.2%

Volume of acid to reach methyl orange end point:66.18c.c. (.116N)

(66.18) (.116) = 7.73 m.e. = .00773 moles.

Percentage Purity of the Nitroamine:

(100) (.00773)/(.00789) = 98.0%

3. Preparation of a Mixture of Hydrolysis Products as Postulated.

A mixture corresponding to the composition of a solution after hydrolysis with 10% NaOH was prepared. On the basis of a 5 gram sample of N-Nitroisopropylurethan (.0284 moles) the following quantities of reagents were employed.

7.72 gr sodium hydroxide

94 c.c. distilled water

2.96 gr. isopropylnitroamine

3.01 gr. sodium carbonate

1.30 gr. ethyl alcohol (absolute)

The mixture was diluted to a volume of 200 c.c. in a volumetric flask. A 50 c.c. aliquot portion was taken and diluted with 50 c.c. of distilled water. It was titrated with standard acid using both indicators and a pH meter. The indicator color changes corresponded with the rapid pH changes as shown by the potentiometer. The HCl used was .567 N. Figure I was constructed by plotting the measured pH against the volume of standard acid added. The calculations for determining percentage hydrolysis were applied to this mixture as follows.

villequivelents of Bane Newbrulland by Nitrosmine:

11.67-3.92 = 7.75 = .00775 moles.

Percentage Furthy of the Mitrosmine:

(100) (.00775)/(.00789) = 98.8%

.o.o81.33: dailog bas egasto lydrem doser of blos to erulov (NJLL.)

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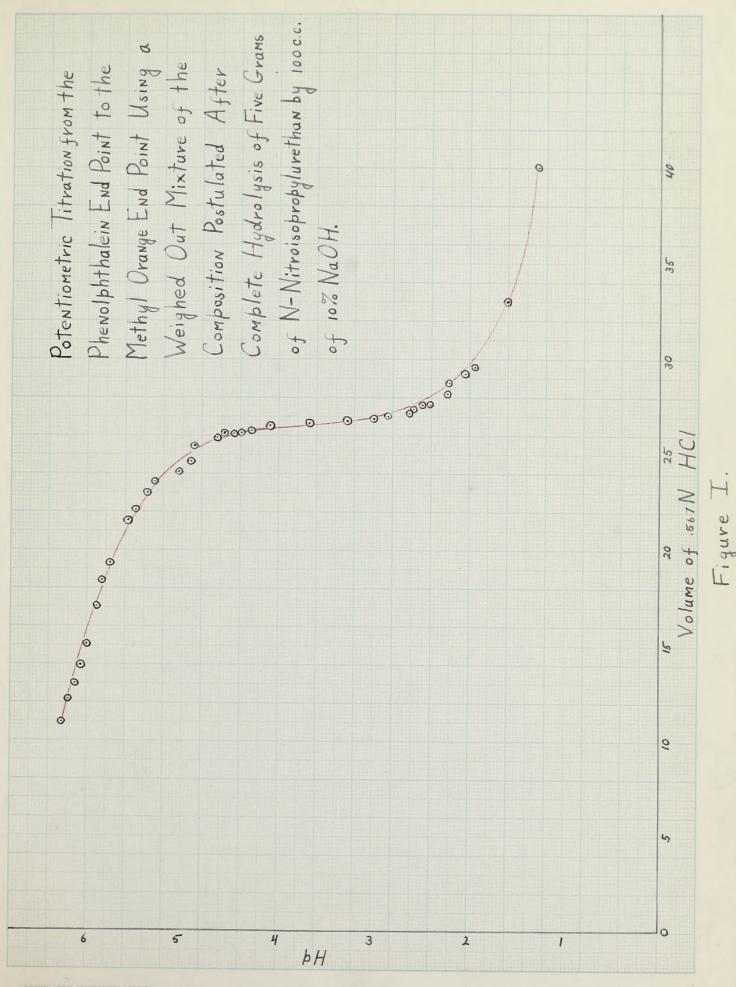
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Weight of sample* 5.000 gr.

Theoretical CO_2 : (5.000) (44/176) = 1.2500 (1.2500)/(44.00) = .00284 moles = 28.4 millimoles of CO_2 In a 50 c.c. sliquot there will be 28.4/4 = 7.10 millimoles Total millimoles to be titrated (sodium salt of nitroamine plus sodium carbonate) 2x7.10 = 14.20

From Figure I we observe that the volume of acid necessary to go from the phenolphthalein end point to the methyl orange end point was 26.6 c.c.

The standard acid employed was .567 N.

$$(26.6) (.567) = 14.7 \text{ millimoles}$$

Percentage Hydrolysis:

$$(100) (14.7) / (14.2) = 103\%$$

Thus it seems evident that the composition of the reaction mixture after hydrolysis is as postulated and that the analytical method employed is correct within the limits of experimental error.

^{*} Quantities of reagents based on this figure

.TR 000.2 *signes to ddniew

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The standard soid employed was .367 M.

selomillim 7.41 = (788.) (8.88)

Percentage Hydrolysis:

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Thus it seems evident that the composition of the respictor wixture after hydrolysis is no postulated and that the analytical method employed is correct within the limits of experimental error.

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IV. ACID HYDROLYSIS

A. Methods Employed:

In acid media the carbon dioxide produced by hydrolytic decomposition of the nitrourethan would of course be insoluble. Consequently it was planned to determine the percentage hydrolysis in acid solution by quantitative measurement of the carbon dioxide evolved from the reaction mixture. Sulfuric acid of varying concentrations was to be used as the hydrolysis medium. Three methods were employed for the collection of carbon dioxide; only one of which proved suitable for its quantitative determination under the conditions of the hydrolyses discussed below.

1. Adsorption on Ascarite.

Ascarite, asbestos particles impregnated with sodium hydroxide, is widely used in the determination of carbon in steel. This substance adsorbs quantitatively all of the carbon dioxide evolved when a small sample of steel is heated to a high temperature.

Accordingly it was thought that the carbon dioxide evolved in the nitrourethan hydrolysis could be collected in this manner.

The apparatus employed was set up as follows: A 500 c.c. threenecked flask, fitted with a gas inlet tube, a reflux condenser and a
thermometer, was employed. The top of the condenser was connected to two
calcium chloride tubes in series and from the second of the calcium chloride
tubes a three foot length of rubber tubing led to a standard type Ascarite
tube supported on a tripod.

To the gas inlet tube were connected in series an ascarite tube, a celcium chloride tube, a bubbling bottle and a nitrogen tank. The nitrogen was passed into the reaction vessel for the purpose of sweeping the

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carbon dioxide out of the flask and through the rest of the system. The calcium chloride tube was for the purpose of drying the nitrogen before it entered the Ascarite tube, for moisture might cause clogging to occur. The Ascarite tube was to remove any carbon dioxide from the nitrogen before it entered the reaction chamber.

One hundred cubic centimeters of sulfuric acid of the desired concentration was placed in the flask and a sample of the nitrourethan (about 10 grams) was weighed into the flask from a small dropping bottle.

The previously weighed Ascerite tube was attached to the end of the system and a slow stream of nitrogen was allowed to pass through. The flask was heated until the thermometer in the liquid registered 130° - 135°C. Heating was then continued for three hours. At the end of this time the carbon dioxide evolved was to be determined directly by the increase in weight of the Ascarite Tube.

Three runs only were made using this method and the following results were obtained: 10% H₂SO₄, 14.2% hydrolysis; 50% H₂SO₄, 98.6% and 115.5% hydrolysis. Examination of the Ascarite tube in the last two runs showed that small droplets of liquid were condensed on the sides of the tube in many places. Also at various points the Ascarite had taken on a dark brown tinge in contrast to its normal cream color. It was evident that some of the hydrolysis products or perhaps the nitrourethan itself was vaporizing and eluding the calcium chloride only to be trapped by the Ascarite. As a result the use of this method was discontinued.

2. Absorption in Barium Hydroxide:

It was thought that the extra weight of the Ascarite tube in the previous experiments might possibly be due to acidic oxides of nitrogen

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resulting from complete decomposition of the nitrourethan and its hydrolysis products by the sulfuric acid. Collection of the carbon dioxide evolved as barium carbonate seemed to offer a solution to this problem.

$$Ba(OH)_2 \neq CO_2 \longrightarrow BaCO_3 \neq H_2O$$

Any barium nitrate formed would be water soluble and not interfere in the gravimetric determination of the carbonate.

The appearatus was set up as for Ascarite adsorption with the exception that the two calcium chloride tubes between the reflux condenser and the receiving vessel were eliminated. The Ascarite tube was replaced by two 250 c.c. conical flasks containing 150 c.c. each of a saturated solution of barium hydroxide (15 grams in 300 c.c. of water). The reaction was carried out as before and after ten minutes a precipitate of barium carbonate began to appear in the absorption flasks. The gas issuing from the terminal flask was shown to be a mixture of nitrogen and carbon dioxide by allowing it to pass through a solution of barium hydroxide in a test tube, during which time a white precipitate of barium carbonate appeared.

The precipitate in the two flasks was collected on a Gooch crucible and dried at 110°C. Application of the appropriate calculations gave 23.7% hydrolysis for three hours refluxing with 50% sulfuric acid.

The low result is undoubtedly due to inefficient absorption of of the carbon dioxide. This could only be remedied by the employment of a large excess of the barium hydroxide solution which probably involves volumes of one or two liters, causing this method to become too unwieldy for quantitative work. This method was also abandoned in favor of that which follows.

3. Absorption in Sodium Hydroxide:

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3. Absorbtion in Sodium Hydroxids:

Since it was shown in the previous experiment that collection in an alkaline solution is fegsible, it was decided to try sodium hydroxide in place of the barium hydroxide. It was expected that the highly concentrated solutions of sodium hydroxide which it is possible to obtain would insure quantitative collection of the carbon dioxide. The carbon dioxide would, of course, be collected as sodium carbonate.

$$2NeOH \neq CO_2 \longrightarrow Ne_2CO_3 \neq H_2O$$

Titration of the mixture to the phenolphthalein end-point would involve the following reactions.

NaOH
$$\neq$$
 HCl \longrightarrow NaCl \neq H2O
Na2CO₃ \neq HCl \longrightarrow NaHCO₃ \neq NaCl

Continued titration with standard hydrochloric acid to the methyl orange end-point would bring about decomposition of the sodium bicarbonate.

NaHCO₃
$$\neq$$
 HCl \longrightarrow NaCl \neq H₂O \neq CO₂

Thus it was planned to titrate the carbon dioxide in a manner similar to the methods employed for basic hydrolysis.

The apparatus employed was identical with that used in the first two attempts with the exception that the absorption vessels in this case were four eight inch test-tubes containing 40 c.c. each of 35% sodium hydroxide solution.

The tubes which conducted the gas into the absorbing medium were drawn to fine capillaries in order to provide maximum surface for the reaction to take place.

At the end of the desired refluxing time, heating was discontinued and nitrogen was allowed to pass through the solution for the next fifteen minutes. The contents of the four test-tubes were then transferred quantitatively to a 500 c.c volumetric flask and diluted to volume with

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NaOH
$$\neq$$
 HOL \rightarrow NeOL \neq H2O NaCL NaCL \neq H2O NaCL

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distilled water. One-hundred cubic centimeter aliquot portions were then titrated to the phenolphthalein end-point with dilute hydrochloric acid and to the methyl orange end-point with standard hydrochloric acid(about .4N).

In all cases studied by this method a white precipitate invariably appeared in sodium carbonate, the solubility product of which had been exceeded in the strongly alkaline solution. It dissolved readily on dilution.

4. Sample Calculation:

Data of the following type were employed for the calculation of the percentage hydrolysis in the runs described under "Absorption in Sodium Hydroxide" above.

Acid Hydrolysis of N-Nitroisopropylurethan

3 hours refluxing with 100 c.c. of 50% $\rm H_2SO_4$

Wt. tube and sample 47.2652

Wt. tube 32.6412

Wt. sample 14.6240

 $14.6240/4^* = 3.6560$ grams of CO_2 available.

3.6560/44 = .08308 = 83.08 millimoles of CO_2

Since the total volume was 500 c.c., in a 100 c.c. aliquot there should be 83.08/5 = 16.61 millimoles.

TITRATIONS

troupeth 1	to This coupons at	ight be formed in and	[]
End	39.52	End	39.46
Start	.09	Start	35
	39.43		39.11

Average: 39.27

* See page 17

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Acid Hydrolysis of M-Mitroisogropyllmethen

3 hours refluxing with 100 c.c. of 50 Hg50a

Wt. tube and sample 47.2652

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14.6240/4 = 3.6560 grams of CO2 available.

Since the total volume was 500 c.c., in a 100 c.c. aliquot there should be 83.08/5 = 16.61 millimoles.

SMOITARTIT

11 29.45 Ind 39.45 and 39.45 and 39.45 and 39.43 and 39.43 and 39.43

Average: 39.27

^{*} See page 17

The standard hydrochloric used was .4012N

$$(39.27)$$
 $(.4012) = 15.8$ millimoles

Thus:

Percentage Hydrolysis (100) (15.8)/(16.6) = 95.2%The results obtained by application of the above calculations are tabulated below. The reactions were carried out at about $130^{\circ}-135^{\circ}$ C.

TABLE V
PERCENTAGE HYSROLYSIS IN ACID MEDIUM

% H ₂ SO ₄	TIME	% HYDROLYSIS
50%	3 hrs.	95.2%
50%	1 hr.	79.8%
50%	$\frac{1}{2}$ hr.	74.4%
20%	6 hrs.	73.5%
10%	8 hrs.	28.7%
5%	8 hrs.	21.5%
5%	8 hrs.	26.0%
50% CH3COOH	4 hrs.	26.3%

B. Tetranitromethane:

When the acid used for hydrolysis was 20% H2SO4 or over, the liquid in the absorption tubes took on an intense yellow color. It was postulated that this might be due to the presence of tetranitromethane in the nitrourethan. This compound might be formed in small quantities by reaction of the acetic anhydride with the fuming nitric acid during nitration of the isopropylurethan.

 $(CH_3CO)_2O \neq 8HONO_2 \longrightarrow 2C(NO_2)_4 \neq 2CO_2 \neq 7HOH$ Hydrolysis of this tetranitromethane would then occur simultaneously with

MSIO4. asw beny stroincorbyd brabasia edT

ceforillin 8.21 = (\$104.) (78.88)

Thus

Percentage Hydrolysia (100) (15.8)/(16.6) \pm 95.2 between the above calculations are tabulated by application of the above calculations are tabulated below. The resultions were carried out at about 150^{0} - 135^{0} C.

PERCENTAGE HYSROLYSIS IN FOTO MEDIUM

атачаоночи у	THIT	408gH X
95.26	3 hrs.	
79.87	I hr.	
74.45	÷ hr.	
73.5%	6 hrs.	
28.7%	8 hrs.	
26.18	say B	
20.05	8 Ars.	
NE. 0S	, and à	

s. Tetrenitromethanet

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(OH) 2 / EHONOS / SC(NOS) 4 2500 / THOH

Hydrolysis of this tetranitromethans would then occur simultaneously with

that of the nitrourethan to yield nitroform.

$$C(NO_2)_4 \neq HOH \longrightarrow H-C(NO_2)_3 \neq HONO_2$$

This nitroform might conceivably pass through the condenser in small quantities and react with the sodium hydroxide to form its sodium salt which is highly colored.

$$H-C(NO_2)_3 \neq NaOH \rightarrow NaC(NO_2)_3 \neq HOH$$

However, a brown ring test on the residue of several of the runs described wwws negative. On this basis it was concluded that if tetranitromethane were present, its amount was negligible.

In order to test the foregoing hypothesis, tetranitromethane was prepared by the method of Chatterway (2).

To 31 grams of nitric acid (sp.gr.1.53) was added gradually 50 grams of acetic anhydride. The flask was cooled so that the temperature did not go above 20°-25°C. The flask was stoppered loosely and allowed to stand at room temperature for about a week. As the reaction proceeded, carbon dioxide was slowly evolved and the colorless mixture became brown due to the presence of oxides of nitrogen. After one week the mixture was poured into 200 c.c. of water. Tetranitromethane separated. The oil was washed with water until it was free from acid.

Chatterway (2.) mentions that tetranitromethane can also be freed from acids by steam distillation although some nitroform is formed in this operation and imparts a bright yellow color. Thus it seems evident that nitroform would assuredly be formed under the conditions employed in the present work.

Four drops (.2c.c.) of the tetranitromethane were refluxed for two hours in the appearatus used for hydrolysis of the nitrourethan. No precipitate appeared in the absorption tubes during this time (See page 26)

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HOH + E(800) OBN - NON + E(800) 3 + HOH

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To 31 grams of static soid (sp.gr.1.53) was added grandelly 50 grams of scatic annydride. The flask was cooled so that the temperature did not go above 200-2500. The flask was coppered loosely and allowed to stand at room temperature for about a week. As the restion proceeded, carbon dioxids was alowly evolved and the colorless mixture became brown due to the presence of oxides of nitrogen. After one week the mixture was poured into 200 c.c. of water. Tetranitromethan separated. The oil was rounded with water until it was free from soid.

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but the solution took on an intense yellow color exectly like that observed when the nitrourethan was hydrolyzed. This time a brown ring test on the hydrolysis medium was positive. Thus we may conclude that the amount of tetranitromethane in the sample of isopropylnitrourethan used is considerably less than .2 c.c.

C. Further Hydrolysis:

It was thought that the nitroamine formed by hydrolysis of the nitrourethan might undergo further hydrolysis to yield the amine and nitric acid.

$$(CH_3)_2CNH-NO_2 \neq HOH \longrightarrow (CH_3)_2CNH_2 \neq HONO_2$$

Although this reaction was shown not to occur to any appreciable extent in basic solution, it seemed desirable to determine whether or not it did take place in acid solution.

Attempts to get a brown-ring test on the acid residues from the various hydrolyses failed, so we may conclude that this reaction does not take place under the conditions herein described.

D. Inhibition:

As mentioned in the introduction, (page 8) it was planned to add certain reagents capable of utilizing the unshared pair on the amino nitrogen in the nitrourethan molecule. It was decided to employ acid of the lowest concentration possible so that there would be less danger of any weak bond being disrupted by the hot acid. The results tabulated on page 28 indicated that probably eight hours refluxing with 5% H₂SO₄ would be suitable conditions for this investigation.

It was found that gentle refluxing could be induced in acid of this low concentration at about 110°C. Accordingly the flask was heated with an oil-bath maintained at 115°C. The thermometer inside the flask was

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omitted.

It was decided to employ stirring, for in some of the test runs it was found that contact between the nitrourethan and the inhibitor could not be effected in the absence of agitation. For example, the nitrourethan floated on the surface of the acid but an inhibitor such as chloroform sank to the bottom so that contact was prevented.

Accordingly a mercury-sealed stirrer was employed. Enough mercury was used in the trap to withstand the pressure of approximately sixteen inches of alkaline solution in the absorption tubes.

Three potential inhibitors were tried and it was thought that they might utilize the unshared electron-pair on the amino nitrogen and thus prevent attachment of the proton (the postulated initial step in the hydrolysis) from occurring.) The equations below illustrate this.

1. Chloroform:

$$NO_{2}O$$

 $(CH_{3})_{2}CH-N-C-O-C_{2}H_{5} \neq H-C-Cl_{3} \longrightarrow (CH_{3})_{2}CH-N-C-O-C_{2}H_{5}$
 $H-CCl_{3}$

2. Cholesterol

$$(CH_3)_2$$
-CH-N-COOC₂H₅ \neq R:Q: H \longrightarrow $(CH_3)_2$ -CH-N-COOC₂H₅
R = Parent hydrocarbon structure of cholesterol.

3. Boric Acid:

$$(CH_3)_2CH-N-CC-O-C_2H_5 \neq B-O H \longrightarrow (CH_3)_2-CH-N-CC-OC_2H_5$$
H

(CH_3)_2CH-N-CC-OC_2H_5 \text{H} O-B-O H

The results obtained on the basis of these postulated mechanisms are tabulated below:

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It was found that contact between the nitrourether and the inhibitor could be found that contact between the nitrourether and the inhibitor could not be effected in the absence of agitation. For example, the nitrourether floated on the surface of the acid but an inhibitor such as obtaclor of the best on the best of the contact was greened.

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Three potential inhibitors were tried and it was thought that they might utilize the unabsred electron-pair on the amino nitrogen and thus or event attachment of the proton (the postulated initial step in the hydrolysis) from occurring.) The equations below illustrate this.

2, <u>Cholesterol</u>
(CH₃)₂-CH-H-2-COO₂H₃ + R · D: H · CH₃)₂-CH-N-COO₂H₃
H O' R

The results obtained on the bests of these postulated mechanisms are tabulated below:

TABLE VI
PERCENTAGE HYDROLYSIS WITH ATTEMPTED INHIBITION

% H ₂ SO ₄ INHIBITOR AMOUNT	TIME % HYDROLYSIS
5% None	7 hrs. 14.9%
5% None	7 hrs. 15.8%
5% CHCl ₃ 7 c.c.(lmd.eg.)	7 hrs. 16.7%
5% Cholesterol 1.5 grams	7 hrs. 15.9%
5% Cholesterol 1.5 grams	7 hrs. 15.9%
5% H ₃ BO ₃ 5 grams	7 hrs. 15.6%

Obviously the reagents employed do not prevent hydrolysis to any degree which is detectable by the methods used.

E. ACID ALCOHOLYSIS:

In an attempt to determine the true mechanism of the acid hydrolysis of isopropylnitrourethan, the following experiments were performed.

Alcoholysis was attempted by passing dry hydrogen chloride gas through an alcoholic solution of the nitrourethan. It was postulated that if alcoholysis proceeded by the mechanism whereby the proton attacks the amino nitrogen atom (page 6), that the products of the reaction would be diethyl carbonate and isopropyl nitroamine.

$$(CH_3)_2$$
-CH-N-C-0-C₂H₅ \neq C₂H₅OH $\xrightarrow{HC1}$ $(CH_3)_2$ -CH-N_H \neq C₂H₅-O-C-0-C₂H₅

On the other hand if the reaction proceeded by the accepted mechanism of ester hydrolysis (page 7) the overall result would be no different products.

In preparation for this investigation, diethyl carbonate was distilled under reduced pressure and was found to have a boiling point of 57° C @ 50mm.

PERCLATAGE HYDROLYSIS WITH ATTEMPTED INHIBITION

ELEVIOROTA J	MIT	TMUCMA	ROTIBLEVI	/ H2804
76.01	7 hrs.		None	
18.81	7 brs.		None) a
hv.ar	eg.) 7 hrs.	7 c.c.(lmd.e	CHOIS	
ne.ar	is V hrs.	l.S gran		5%
15.9%	s 7 hre.	1.5 gran	Cholesterol	
15.6%	s 7 hrs.		H ₃ B0 ₃	

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E. MCIO ALCOHOLYBIS:

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The reaction was carried out as follows:

Twenty grams of isopropylnitrourethan was placed in a 200 c.c. round bottomed flask and 50 c.c. of absolute ethanol was added. A current of dry HCl was passed through this mixture for a period of two hours. At first a good deal of heat was evolved and gentle refluxing was evident in the solution. After about thirty minutes the exothermic reaction subsided and at the end of the two hour period the flask and its contents were at room temperature.

The mixture was transferred to a Claisen flask and distilled under reduced pressure. The first fraction, ethyl alcohol passed over at 33°C @ 50 mm. Then there was a sharp rise to approximately 85°C. Since there was no fraction boiling at 57°C (diethyl carbonate) and none boiling over 90°C (isopropylnitroamine) we may conclude that these substances were not present.

Thus it would seem that the mechanism of nitrourethan hydrolysis is closely similar to that accepted for ester hydrolysis.

When a current of dry HCl was passed through absolute ethanol a good deal of heat was evolved, indicating that the heat observed was merely the heat of solution of HCl in ethanol.

the mixture allowed to soul to room impurators. Two or tires outle date

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It was transferred to a two-likes reportery functions and extracted such

apparent within sulfate and the other man distinct as a some main. To

residue mis a light brancalit.

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The reaction was carried out as follows:

Trenty grams of isomopylnitrourelden was placed in a 200 c.c. round bottom100 grams and 50 c.c. of absolute ethenol was added. A current of dry ECL
was passed through this mixture for a period of two hours. At first a good
deal of heat was evolved and gentle refluxing was evident in the solution.

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V ISOPROPYLNITROAMINE:

A. Isolation:

As was predicted in the introduction to this Thesis (page 6), isopropylnitroamine was found to be one of the producte of the hydrolysis of isopropylnitrourethan. It was extracted from both acidic and basic hydrolysis mixtures by shaking with ether. The basic mixtures were acidified before ether extraction. When distilled under reduced pressure the compound passed over at the temperature recorded by Thomas (12.), 90° @ 10mm.

B. Preparation:

The procedure which was employed for the hydrolysis of large quantities of N-Nitroisopropyl urethan is as follows.

One equivalent of isopropylnitrourethan (176gr.) was placed in a one liter round-bottomed flask containing 4 equivalents of sodium hydroxide in the form of a 35% solution. (160 grams of NaOH in 290 c.c. of water). Three equivalents of sodium hydroxide are necessary for complete hydrolysis (page 16), the fourth equivalent was added to insure rapidity of hydrolysis.

The flask was then connected to a reflux condenser and was heated for four hours, At the end of this time the heating was discontinued and the mixture allowed to cool to room temperature. Two or three cubic centimeters of methyl orange solution was added and the solution was acidified with concentrated hydrochloric acid until a bright red color was obtained.

The acidic mixture was then allowed to cool to room temperature. It was transferred to a two-liter separatory funnel and extracted with 3-300 c.c. portions of ether. The ether layer was dried with 50 grams of anhydrous sodium sulfate and the ether was distilled on a steam bath. The residue was a light brown oil.

The oil was distilled under reduced pressure and passed over at

W ISOPROPYLNITROALINE:

A. Isolotlon:

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The flask was then connected to a reflux condenser and was hested for four hours. At the end of this time the heating was discontinued and the mixture allowed to cool to room temperature. Two or three cubic centrication was another to see the and the solution was solutified and the solution was obtained. With concentrated bydrochloris acid until a bright red color was obtained.

It was transferred to a two-liter separatory funnel and extracted with 50 grams of 3-300 o.c. portions of stner. The other layer was distilled on a steem beth. The analydrous sodius sulfate and the stner was distilled on a steem beth. The residue was a light brown oil.

The oll was distilled under reduced pressure and passed over at

89°C under a pressure of 8mm. The product, isopropylnitroamine, was a water-white liquid with a faintly sweet odor.

The molecular weight of isopropylnitrosmine is 104. The yield was 79 grams (76%).

When 288 grams of isopropylnitrourethan was hydrolyzed by this method in a five liter flask a yield of nitroamine corresponding to only 40% of the theoretical was obtained. Evidently the condenser was not efficient enough to take care of the large boiling surface.

Isopropylnitroamine has been extracted from some of the acidic hydrolysis mixture and has been identified by its boiling point and odor. The same method that was used for extraction of the nitroamine from basic media was employed. Of course acidification is unnecessary.

C. Preparation of Derivatives:

Aside from metallic salts prepared by Thomas (12.) and others (page 4) no solid derivatives suitable for identification of nitroamines have been recorded in the literature. Thus it seemed desirable to attempt to prepare a series of compounds with this purpose in mind.

Although the nitrosmine is an acidic substance it was thought that it might react with the acid chlorides which are ordinarily employed for the preparation of solid derivatives of primary and secondary amines. Accordingly attempts were made to bring about a reaction between the nitromaine and such acidic reagents as benzenesulfonyl chloride, p-bromobenzenesulfonyl chloride and benzoyl chloride. Failing to effect a reaction with any of these reagents, basic reagents were turned to. Two of these reagents, morpholine and piperazine yielded satisfactory solid salts. The results of this investigation are discussed more completely below.

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1.Benzenesulfonyl chloride (10.)

Equivalent amounts of benzenesulfonyl chloride and isopropylnitroamine were mixed with 50 c.c. of 10% sodium hydroxide solution. On shaking, much heat was evolved. It was thought that the following reaction might have occurred.

 $C_6H_5SO_2C1 \neq (CH_3)_2CH-N \xrightarrow{NO_2} (CH_3)_2CH-N \xrightarrow{NO_2} SO_2-C_6H_5 \neq HC1$ However, precipitation did not occur on cooling the reaction mixture in an ice salt bath and no precipitate appeared when a small portion of the mixture was acidified in a test-tube.

The reaction mixture was then extracted with three 20 c.c. portions of ether. The ether extract was set aside to evaporate. No residue remained in the evaporating dish after evaporation of the ether. The heat evolved must have been merely a result of the hydrolysis of the acid chloride. Similar observations were made on a blank run. The N-Nitrobenzene sulfonamide of isopropyl nitroamine has been prepared by Zsolonina (17.) by reacting the isopropyl amine with benzenesulfonyl chloride and nitrating the resulting product. The compound had a melting point of 34°-35°C.

2. Benzoyl chloride: (10.)

The same procedure that was used with benzenesulfonyl chloride was followed with benzoyl chloride. Evaporation of the ether extract again yielded no residue.

3. p-Bromobenzenesulfonyl chloride: (10.)

Two grams of isopropylnitroamine and five grams of p-bromobenzene sulfonyl chloride were added to 30 c.c of 10% NaOH. No reaction occurred in the cold, the solid acid chloride merely settling to the bottom of the flask.

On heating the acid chloride melted and slowly went into solution (about 15 min.).

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Equivalent smounts of benzenesual long chloride and isomorphic.

And a solution of 10 sodium nydpoxide solution. On shaking, such heat was avolved. It was thought that the following restrion might have occurred.

C6H3802C1 / (CH3)2CH-N 102 CH3)2CH-N 802-C6H3 / HC1

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3. p-Bromobenzeneaulfonyl chloride: (10.)

Two grams of isognopylnitrosmine and five grams of p-bromobensene sulfonyl chloride were added to 30 c.c of 10% NaOH. No reaction occurred in the cold, the solid acid chloride merely settling to the bottom of the flank.

On heating the acid chloride melted and slowly went into solution (about 15 min.).

When the acid chloride had dissolved completely, the solution was still alkaline.

On cooling of the reaction mixture white crystals separated. These crystals were soluble in water, insoluble in ether and would not burn; suggesting a salt rather than a sulfonamide. The crystals were filtered and dried. The three possible substances which might precipitate from such a reaction mixture are the following:

Br-C₆H₅-SO₂-ONa, Br-C₆H₅-SO₂-N(NO₂)-(CH₃)₂, (CH₃)₂CH-N(NO₂)Na

It is obvious that qualitative analysis for the elements nitrogen, sulfur and bromine would serve to distinguish the product. Accordingly sodium fusion was performed and these elements were tested for using the methods described by Shriner and Fuson (10.).

The qualitative tests indicated the presence of sulfur and bromine only. The crystals were therefore the sodium salt of p-bromobenzenesulfonic acid, Br-C₆H₅-SO₂-ONa, and it is clear that the only reaction which occurred was hydrolysis of the acid chloride.

Similar observations were made on a blank run. The blank run was carried out as just described above with the exception that the isopropylnitroamine was withheld

4. Morpholine:

After failing in attempts to bring about reactions with various acidic reagents which usually react with amines it was decided to try basic reagents in the hope that they would yield salts with the acidic nitro-amine.

The first of the basic reagents employed was morpholine. It was decided to mix ethereal solutions of the two reactants and if a salt like

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Hr-OgHg-SO2-ONE, Br-CgH5-SO2-N(NO2) (CH2)2. (CH2)2CH-N(NO2)Ne.

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A. Morgholines

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The first of the besides two resolutions of the two resolution and if a salt like

derivative formed, it was thought that it would precipitate. Accordingly equal volumes (1 c.c.) of morpholine and isopropylnitroamine were dissolved separately in 3 c.c. portions of ether. The two solutions were mixed and a rather vigorous exothermic reaction took place causing the ether to boil. The mixture became rather viscous but precipitation did not occur. It is noteworthy that the proportion of reactants employed corresponds to a considerable excess of the nitroamine. The mixture was set aside to evaporate and faintly yellow colored crystals were obtained. The crystals were washed with ether by suction. M.P. 65-68°C.

The following procedure was employed for preparing this compound in larger quantity and greater degree of purity. Since an excess of nitro-amine seemed to retard precipitation, it was decided to employ an excess of morpholine, the latter being more readily volatile than the nitroamine. The molecular weight of isopropylnitroamine is 104, that of morpholine 87.

104/87 = 1.21 gr. nitrosmine/gr.morpholine

In order to insure an excess of morpholine five grams of this compound were added to 50 c.c. of ether and five grams of isopropylnitroamine were added dropwise. The reaction was observed to be exothermic but in this case not violent enough to bring about ebullition of the solvent. Precipitation did not occur immediately. The mixture was set aside and after about ten minutes precipitation began to take place in such a rapid manner that little waves were created on the surface of the liquid. The crystals were filtered off by suction and washed with two 20 c.c. portions of ether. The yield was nine grams (about 100%).

<u>Properties</u>: Soluble in water, insoluble in ether. Crystals are scaly in appearance. Water solutions of this compound are neutral to litmus, methyl orange and phenolphthalein. M.P. 69°-70°C.

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Properties: Soluble in water, incoluble in ether. Crystals are scaly in appearance. Water solutions of this compound are neutral to liteus, methyl orange and phenolphthalein. M.P. 690-700C.

It is thought that the equation for the reaction may be written as follows.

Actually an acid-base reaction has taken place and the result is a salt.

The compound has a molecular weight, as calculated from the formula, of 191.

Results of analysis for carbon and hydrogen are shown below.

	Carbon	Hydrogen	
Calculated	44.0%	8.9%	
Observed	43.77%	9.12%	
Observed	43.81%	9.30%	

5. Piperazine:

A similar reaction was effected with piperazine. The reaction, however, had to be carried out in alcohol because the piperazine is insoluble in ether. There are two possible reaction products in this case since the piperazine ring contains two secondary amino groups. The reaction can theoretically proceed by either of the following two paths.

$$(1.) \quad CH_{3} \quad NO_{2} \quad CH_{2}-CH_{2} \quad N-H \quad N$$

The fact that the reaction product was neutral in its water solutions to litmus is good evidence for compound II because compound I which has one free amino group as does morpholine whould be basic to litmus as is morpholine.

The method of preparing the compound was as follows: Three grams of piperazine were dissolved in 40 c.c. of ethyl alcohol since piperazine is

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Actually in sold-base reaction has taken place and the result is a salt.

The compound has a molecular weight, as calculated from the formula, of 191.

Results of analysis for carbon and hydrogen are shown below.

Hydrogen	Garbon	
70.8	10.00	
721.6	43.77%	
208.6	43.81%	
		Pineragines

A similar resultion was effected with piperasine. The resultion,

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theoretically proceed by either of the following two meths.

The fact that the reaction product wes neutral in its voter solutions to liters is good evidence for compound II because compound I which has one free swing group as does morpholine whould be easie to liters as is morpholine. The method of preparing the compound was as follows: Three grams of piperssine is

insoluble in ether. Vigorous stirring was necessary to effect complete solution. Nine grams of isopropylnitroamine (enough to react with both amino groups) was added to the solution. The mixture was then poured into 500 c.c. of ether and voluminous precipitation occurred. The mixture was filtered by suction and the feathery crystals were washed with two 20 c.c. portions of ether. The yield was about four grams (57% or 36% depending upon structure). An additional two grams of product was obtained on evaporation of the ether-alcohol mixture. (Total yield 65%). This last compound melted around 113°C whereas the precipitated compound melted at about 114°C. The molecular weights postulated are I, 190; II, 294.

Results of carbon-hydrogen analysis are as follows:

		Carbon	Hydrogen
Calculated	I .	44.0%	9%
Calculated	II	40.8%	8.85%
Observed		40.89%	9.22%
Observed		40.99%	9.06%

Thus we may conclude that the structure of the compound is that which corresponds to two moles of isopropylnitroamine per mole of piperazine.

The compounds employed in this attempted inhibition were chicrafers, choice

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The altropathes employed to this work was propored by restline

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Results of cerbon-hydrogen unelysis ere as follows:

Hydrogen	Carbon	
	70.44	Calculated
3,88.9	40.85	
Nas,e	he8.04	DevreedO
9.06	40,99%	

Thus we may conclude that the structure of the compound is that which corresponds to two moles of isographinitrosmine per mole of piperarias.

VI SUMMARY

The information recorded in the previous pages may be summarized as follows.

N-Nitroisopropylurethan has been subjected to hydrolysis in both basic and acidic media, varying the concentration of the hydrolyzing agent as well as the time of contact with this reagent.

As a general rule the nitrourethan is more easily hydrolyzed by acids than by bases, i.e. in a given time interval a given concentration of sodium hydroxide will give a greater degree of hydrolysis than the same concentration of sulfuric acid.

The mechanism of this hydrolytic splitting has been discussed in detail and it was concluded that probably the attack of the acidic and basic reagents takes place at the carbonyl group as in ordinary ester hydrolysis rather than at the amino nitrogen atom as was first postulated for acid hydrolysis.

In order to test the postulated mechanism of acid hydrolysis, certain reagents were to be added to the hydrolysis mixtures in an attempt to form addition compounds, or compounds containing hydrogen bonds with the amino nitrogen atom of the nitrourethan. In all cases the percentage hydrolysis was the same as that in the absence of a potential inhibitor.

The compounds employed in this attempted inhibition were chloroform, cholesterol and boric acid. Since no measurements were made to determine whether or not actual compound formation took phace, we can only say that probably hydrolysis in acid media is not initiated by attack of a proton at the amino nitrogen atom.

The nitrourethan employed in this work was prepared by reacting equivalent quantities of ethylchlorocarbonate and isopropylamine in the

The information recorded in the previous pages may be summerized

hesic and soldic media, verying the concentration of the hydrolysing agent as well as the time of context with this reseast.

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The nitrourethan employed in this work was prepared by respilar

presence of enough sodium hydroxide to take care of all of the hydrogen chloride evolved.

The nitration was then carried out by adding the urethan to a mixture of fuming nitric acid and acetic anhydride containing a 50% excess of fuming nitric acid and sufficient acetic anhydride to react with all of the water in the acid and all of the water formed in the reaction.

The products of hydrolysis were determined to be isopropylnitroamine, carbon dioxide and ethyl alcohol. The evolution of carbon dioxide
was employed as the basis for the analytical procedure in the determination
of the degree of hydrolysis in both acidic and basic media. The basic solution was diluted to volume, aliquots taken, and these aliquots titrated
with standard HCl to the phenolphthalein end-point to neutralize all excess
sodium hydroxide and to the methyl orange end-point to determine the carbon
dioxide evolved. Several runs appeared to give values in the vicinity of
200% hydrolysis until it was realized that the sodium salt of the isopropylnitroamine, which was present in an amount equivalent to the carbon dioxide,
was being titrated simultaneously. Calculations made on this basis gave
logical values for the percentage hydrolysis.

Three methods were employed for collecting the carbon dioxide evolved from the acidic hydrolysis mixtures: adsorption on "Ascarite", absorption in berium hydroxide solution and absorption in 35% sodium hydroxide solution. Only the latter method proved to be satisfactory for quantitative collection of the carbon dioxide. The titrations were carried out as just described for basic hydrolysis with the exception, of course, that the nitromine did not interfere in the titration.

A yellow impurity which appeared in the sodium hydroxide absorption tubes was shown to be the sodium salt of nitroform. The nitroform resulted

presence of enough sodium hydroxide to take care of all of the hydrogen

The nitration was then certied out by adding the wrethen to a nixture of fuming nitric acid and acetic anhydride containing a JOE excess of
fuming nitric acid and aufficient acetic unhydride to react with all of the
water in the acid and all of the water formed in the reaction.

The moducts of hydrolysis were determined to de isomopylnitrosmine, carbon dioxide and ethyl slochol. The evolution of carbon dioxide
was employed as the basis for the entlytical procedure in the determination
of the degree of hydrolysis in both acidic and basic medis. The basic solution was diluted to volume, aliquote taken, and these aliquote fitrated
with standard HOI to the phenolybthalein end-point to neutralize all excess
sodium hydroxide and to the methyl orange end-point to determine the carbon
dioxide evolved. Several runs appeared to give values in the vicinity of
alignment, which was present in an amount equivalent to the carbon dioxide.
The baing titrated simultaneously. Desculations made on this basic gave
logical values for the percentage hydrolysis.

Three methods were employed for collecting the cerbon dioxide evolved from the soldic hydrolysis mixtures: adsorption on "Ascarite", absorption in berium hydroxide solution and absorption in 25, sodium hydroxide solution. Only the latter method proved to be satisfactory for quantitative
collection of the carbon dioxide. The titrations were carried out as just
described for basic hydrolysis with the exception, of course, that the nitroemine did not interfere in the titration.

A yellow importity which appeared in the sodium hydroxide absorption tubes was shown to be the sodium selt of nitroform. The nitroform resulted

from hydrolysis of tetranitromethane present in minute amounts as an impurity in the nitrourethan and was carried over with the carbon dioxide. The tetranitromethane resulted from a reaction between the nitric acid and the acetic anhydride during the nitration of the isopropylurethan.

Isopropylnitroamine was separated from the hydrolysis mixtures by first acidifying them to methyl orange if they were not acid already and then extracting with ether. The ether was removed by distillation on a steam bath and the nitroamine was distilled in a vacuum, boiling point 89°C @ 8 mm.

The substance is acidic and when titrated with standard sodium hydroxide it gave a neutral equivalent of 104, corresponding to the formula $(CH_3)_2$ -CH-NH(NO₂).

Attempts were made to prepare derivatives of isopropylnitroamine.

Acidic reagents such as benzoyl chloride and benzenesulfonyl chloride did

not appear to react but two basic reagents, morpholine and piperazine, gave
satisfactory products.

The morpholine salt had a melting point of 69° - 70° C and gave an analysis of 43.77% carbon and 9.12% hydrogen corresponding to a formula $67H_{17}N_{3}O_{3}$, or one mole of nitroamine per mole of morpholine.

The piperazine salt had a melting point of 114° C and gave an analysis of 40.9% carbon and 9.0% hydrogen corresponding to a formula $c_{10}^{\text{H}}_{26}^{\text{N}}_{6}^{\text{O}}_{4}$, or two moles of nitroamine per mole of piperazine.

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